

Poster Presentation

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Structural insights into DNA repair by RNase T

Y. Hsiao¹, H. Yuan²

¹National Chiao Tung University, Department of Biological Science and Technology, Hsinchu, Taiwan, ROC., ²Institute of Molecular Biology, Academia Sinica, Taipei, Taiwan, ROC.

DNA repair is generally accomplished by a coordinated effort via several types of DNA enzymes, including endonucleases, exonucleases, helicases, polymerases and ligases. Among all these DNA enzymes, the molecular functions of exonucleases, which bind at the 3' or 5' end of DNA and cleave one nucleotide at a time, are least understood in how they select DNA substrates for binding and trimming. Here we show that the DEDDh family exonuclease RNase T is critical for *Escherichia coli* resistance to various DNA damaging agents and UV radiation. RNase T specifically trims the 3' end of structured DNA, including bulge, bubble and Y-structured DNA, and it can work with Endonuclease V to restore the deaminated base in an inosine-containing heteroduplex DNA. Our crystal structure analyses further reveal how RNase T recognizes the bulge DNA by inserting a phenylalanine into the bulge, and as a result the 3' end of blunt-end bulge DNA can be digested by RNase T. In contrast, the homodimeric RNase T interacts with the Y-structured DNA by a different binding mode via a single protomer so that the 3' overhang of the Y-structured DNA can be trimmed closely to the duplex region. Our data suggest that RNase T likely processes bulge and bubble DNA in the Endonuclease V-dependent DNA repair, whereas it processes Y-structured DNA in UV-induced and various other DNA repair pathways. This study thus provides mechanistic insights for RNase T and thousands of DEDDh-family exonucleases in DNA 3'-end processing.

[1] Hsiao, Y.Y., Duh, Y., Chen, Y.P., Wang, Y.T. & Yuan, H.S. (2012). How an exonuclease decides where to stop in trimming of nucleic acids: crystal structures of RNase T-product complexes. *Nucleic Acids Res.* 40, 8144-8154., [2] Hsiao, Y.Y., Yang, C.-C., Lin C. L., Lin, J. L. J., Duh, Y. and Yuan, H. S. (2011). Structural basis for RNA trimming by RNase T in stable RNA 3'-end maturation. *Nat Chem Biol* 7, 236-243.

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